

Appl. No. 09/833,328  
Amdt. dated March 15, 2005

PATENT

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Currently amended) A composition exhibiting vWF protease activity comprising at least one single isolated peptide chain having a molecular weight from about 180 kD to about 120 kD as determined by SDS-PAGE under reducing conditions and comprising the amino acid sequence AAGGILHLELLV (~~SEQ ID NO:1~~)(SEQ ID NO:1), wherein the peptide chain is obtained from human plasma.

2. (Original) A composition according to claim 1 wherein said sequence is located at the N-terminus of the peptide chain.

3. (Original) A composition according to claim 1 wherein said peptide chain has a molecular weight of about 180 kD.

4. (Original) A composition according to claim 1 wherein said peptide chain has a molecular weight of about 170 kD.

5. (Original) A composition according to claim 1 wherein said peptide chain has a molecular weight of about 160 kD.

6. (Original) A composition according to claim 1 wherein said peptide chain has a molecular weight of about 120 kD.

7. (Canceled)

8. (Original) A composition according to claim 1 wherein said composition cleaves vWF at the peptide bond 842Tyr-843Met.

9. (Currently amended) A composition according to claim 1 wherein said composition retains activity in the presence of the a serine protease inhibitor diisopropyl fluorophosphate and or a calpain protease inhibitor having the structure Z-Leu-Leu-Tyr-CHN<sub>2</sub>, where Z is carbobenzyloxy.

10. (Currently amended) A composition according to claim 9, wherein said protease inhibitor is diisopropyl fluorophosphate-fluorophosphates.

Appl. No. 09/833,328  
Amdt. dated March 15, 2005

PATENT

11. (Original) A composition according to claim 9, wherein said calpain protease inhibitor is Z-Leu-Leu-Tyr-CHN<sub>2</sub>.
12. (Currently amended) A composition according to claim 1 wherein said peptide chain further comprises the amino acid sequence AVGPDVFQAHQEDTERYVLTNLNI GAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINPEDDTPG HADLVLYTTRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTI (~~SEQ ID NO:15~~) (SEQ ID NO:15) following the sequence AAGGILHLELLV (SEQ ID NO:1) (~~SEQ ID NO:1~~).
13. (Original) A composition according to claim 1, further comprising Ca<sup>2+</sup>, Sr<sup>2+</sup> or Ba<sup>2+</sup> ions.
14. (Previously presented) A composition according to claim 1, further comprising Ca<sup>2+</sup> ions in a concentration of about 1 to 10<sup>6</sup> per selected polypeptide molecule.
15. (Original) A composition according to claim 1, wherein said composition is essentially free of vWF or vWF fragments.
16. (Original) A composition according to claim 1, further comprising clusterin or an analog or derivative thereof.
17. (Currently amended) An isolated polypeptide exhibiting vWF activity, having a molecular weight between 180 kD and 120 kD as determined by SDS-PAGE under reducing conditions and comprising the amino acid sequence AAGGILHLELLV (SEQ ID NO:1), wherein the polypeptide is obtained from human plasma.
18. (Currently amended) presented An isolated polypeptide according to claim 17, wherein said polypeptide comprises the amino acid sequence AVGPDVFQAHQEDTE RYVLTNLNI GAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTI NPEDDTPG HADLVLYTTRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGV TI (~~SEQ ID NO:15~~) (~~SEQ ID NO:15~~) directly following the sequence AAGGILHLELLV (SEQ ID NO:1).
19. (Original) An isolated polypeptide according to claim 18 having a molecular weight of about 170 kD.

Appl. No. 09/833,328  
Amdt. dated March 15, 2005

PATENT

20. (Original) An isolated polypeptide according to claim 18 having a molecular weight of about 160 kD.
21. (Original) An isolated polypeptide according to claim 18 having a molecular weight of about 120 kD.
22. (Canceled)
23. (Original) A vWF cleaving complex comprising a polypeptide according to claim 18 and a divalent ion selected from the group consisting of  $\text{Ca}^{++}$ ,  $\text{Sr}^{++}$  and  $\text{Ba}^{++}$ .
24. (Original) A vWF cleaving complex according to claim 23 wherein the divalent cation is  $\text{Ca}^{++}$ .
25. (Previously presented) A vWF cleaving complex according to claim 23, further containing vWF.
26. (Previously presented) A composition comprising a polypeptide according to claim 17.
27. (Canceled)
28. (Canceled)
29. (Previously presented) An isolated polypeptide according to claim 18, wherein the amino acid sequence is encoded by the polynucleotide set forth in SEQ ID NO: 3.
30. (Currently amended) An isolated polypeptide having vWF protease activity wherein said polypeptide is obtained from human plasma and comprises the amino acid sequence AAGGILHLELLVAVGPDVFQAHQEDTERYVLTNLNIGAELLRDP SLGAQFRVHLVKMVLTEPEGAPNITANLTSSLLSVC GWSQTINPEDDTDPGHADLVLYTTRFDLELPDGNRQVRGVTQLGGACSP TWSCLITEDTGFDLGVTI (SEQ ID NO:4)(~~SEQ ID NO:4~~).
31. (Previously presented) An isolated polypeptide according to claim 30 wherein said polypeptide is encoded by a polynucleotide sequence set forth in SEQ ID NO: 3.
- 32-35. (Canceled)